

## PATENT COOPERATION TREATY

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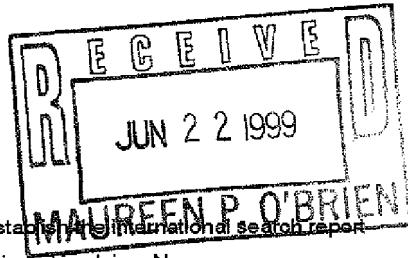
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## INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

<p>Date of mailing (day/month/year) <u>26/05/1999</u></p> <p><b>PAYMENT DUE</b> within <u>45</u> weeks/days from the above date of mailing</p> <p>International filing date (day/month/year) <u>14/01/1999</u></p> <p>Applicant <b>DU PONT PHARMACEUTICALS COMPANY</b></p>	
<p><b>DOCKETED: 6/2/99</b> <b>Due Date: 7/10/99</b></p> <p><b>No Action Required:</b> _____</p>	
<p>1. This International Searching Authority</p> <p>(i) considers that there are <u>3</u> (number of) inventions claimed in the international application covered by the claims indicated below/on the extra sheet:</p> <p>and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below/on the extra sheet:</p> <p>(ii) <input checked="" type="checkbox"/> has carried out a partial international search (see Annex) <input type="checkbox"/> will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.: <b>1-23 in part, 36-44</b></p> <p>(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid</p> <p>2. The applicant is hereby invited, within the time limit indicated above, to pay the amount indicated below:</p> <p><u>DEM 2.198,35</u> x <u>2</u> = <u>DEM 4.396,70</u> Fee per additional invention number of additional inventions total amount of additional fees</p> <p>Or, <u>EUR 1.124,00</u> x <u>2</u> = <u>EUR 2.248,00</u></p> <p>The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.</p> <p>3. <input type="checkbox"/> Claim(s) Nos. _____ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.</p>	



Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer <b>Claudia Aragone</b>
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This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-23 in part, and 36-44

The process for preparing a phospholipid suspension as described in claims 1-23, and the phospholipid suspension thus obtained.

2. Claims: 1-23 in part, and 24-28

The process for preparing a perfluorocarbon-containing contrast agent according to these claims.

3. Claims: 29-35

The process for the preparation of a lipid blend according to these claims.

The problems underlying the present application are: 1. a process for the preparation of a phospholipid suspension, and 2. the preparation of a lipid blend. The solution to the first problem is detailed in claims 1-28, giving rise to phospholipid suspensions according to claims 36-44; the solution to the second problem is given in claims 29-35.

The only technical feature linking these 2 problems and their solution is to be found in the components constituting the lipid blend.

Not only lipid blends are known, as is illustrated by several documents mentioned in the search report: the most preferred lipid blend, i.e. DPPA:DPPC:DPPE-MPEG5000 = 10:82:8 is described in WO-A-96/31196: see the beginning of the example section, and example 1.

Although the applicant might argue, that the lipid blend prepared according to claims 29-35 is different, there is no indication of such difference in the present application. Moreover, the wording of the claims does not exclude the use of the same lipid blend, but prepared in another way.

WO-A-96/31196 thus anticipates the technical feature linking the different subjects contained in the present application. Therefore, this technical feature can no longer serve as special technical feature in the sense of Rule 13 PCT, linking the different subjects together.

Within the preparation of the liposomes, a further objection for lack of unity has to be raised. Indeed, the process according to claims 1-23 can be distinguished from the process according to WO-A-96/31196 by the fact, that the organic solvent is not evaporated before the

aqueous solution is added.

Yet, this feature is well-known to the skilled person: see Liposome Technology, Volume 1, page 29-35. Even in the introductory paragraph of this document, such techniques are described. This document reflects the knowledge of the skilled person. Therefore, even if the presently claimed process is formally novel, its distinguishing feature is based on standard knowledge of the skilled person, and therefore, this technical feature can no longer serve as special technical feature in the sense of Rule 13 PCT, linking the different subjects together.

As the process according to claims 24-28 can be further distinguished from the process according to WO-A-96/31196, combined with standard knowledge of the skilled person, by a different way in which the perfluorocarbon is added, this process is to be considered as a different subject.

Since there is no other technical feature, that could fulfil the role of special technical feature in the sense of Rule 13 PCT, the present application lacks unity of invention, containing the subject-matters as listed.

As searching the remaining subjects would have caused a major supplementary searching effort, a search has been performed for the first subject only.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206**

Claims Nos.: 1-23 and 36-44 in part

In view of the large number of compositions, which are defined by the general definition in the claims, the search had to be restricted for economic reasons. The search was limited to the compositions for which pharmacological data was given and/or the compositions mentioned in the claims, and to the general idea underlying the application (see guidelines, Chapter III, paragraph 2.3).